

In the Claims

Please amend claims 1, 4-9 and 17-42 as follows.

isolate

1. (3 Times Amended) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin):

C¹ the mutant comprising an amino acid substitution at aspartic acid-12 of SEQ ID NO: 2, tyrosine-15 of SEQ ID NO: 2, tyrosine-17 of SEQ ID NO: 2, histidine-35 of SEQ ID NO: 2, asparagine-38 of SEQ ID NO: 2, or substitution at more than one of these amino acids.

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4. (3 Times Amended) The mutant SPE-C toxin of claim 1, wherein the amino acid substitution comprises:

the substitution of aspartic acid-12 of SEQ ID NO: 2 to alanine, glutamic acid, asparagine, glutamine, lysine, arginine, serine, or threonine;

the substitution of tyrosine-15 of SEQ ID NO: 2 to phenylalanine, alanine, glycine, serine, or threonine;

the substitution of tyrosine-17 of SEQ ID NO: 2 to phenylalanine, alanine, glycine, glutamic acid, lysine, arginine, aspartic acid, serine, or threonine;

C¹⁰ the substitution of histidine-35 of SEQ ID NO: 2 to phenylalanine, alanine, glycine, glutamic acid, lysine, arginine, aspartic acid, tyrosine, phenylalanine, serine, or threonine;

the substitution of asparagine-38 of SEQ ID NO: 2 to alanine, aspartic acid, glutamic acid, lysine or arginine; or

substitution at more than one of these amino acids.

5. (3 Times Amended) The mutant SPE-C toxin of claim 4, wherein the amino acid substitution comprises:

the substitution of aspartic acid-12 of SEQ ID NO: 2 to alanine,

the substitution of tyrosine-1 of SEQ ID NO: 2 to alanine,

the substitution of tyrosine-17 of SEQ ID NO: 2 to alanine,

the substitution of histidine-35 of SEQ ID NO: 2 to alanine,

the substitution of asparagine-38 of SEQ ID NO: 2 to aspartic acid; or

C⁸ substitution at more than one of these amino acids.

C⁹ 6. (Twice Amended) The mutant SPE-C toxin of claim 1, wherein the amino acid substitution comprises substitution of tyrosine-15 of SEQ ID NO: 2 and asparagine-38 of SEQ ID NO: 2.

C¹⁰ 7. (Twice Amended) The mutant SPE-C toxin of claim 6, wherein the substitutions are tyrosine-15 of SEQ ID NO: 2 to alanine and asparagine-38 of SEQ ID NO: 2 to alanine.

C¹¹ 8. (Twice Amended) The mutant SPE-C toxin of claim 1, wherein the amino acid substitution comprises substitution of tyrosine-17 of SEQ ID NO: 2 and asparagine-38 of SEQ ID NO: 2.

C¹² 9. (Twice Amended) The mutant SPE-C toxin of claim 8, wherein the substitutions are tyrosine-17 of SEQ ID NO: 2 to alanine and asparagine-38 of SEQ ID NO: 2 to alanine.

17. (Twice Amended) The mutant SPE-C toxin of claim 1, wherein the amino acid substitution comprises:

the substitution of tyrosine-15 of SEQ ID NO: 2 to alanine or serine;

the substitution of tyrosine-17 of SEQ ID NO: 2 to alanine or serine;

the substitution of asparagine-38 of SEQ ID NO: 2 to serine or alanine;

C¹³ the substitution of tyrosine-15 of SEQ ID NO: 2 to serine or alanine and of asparagine-38 of SEQ ID NO: 2 to serine or alanine;

the substitution of tyrosine-17 of SEQ ID NO: 2 to serine or alanine and of asparagine-38 of SEQ ID NO: 2 to serine or alanine;

the substitution of aspartic acid-12 of SEQ ID NO: 2 to alanine;

the substitution of asparagine-38 of SEQ ID NO: 2 to aspartic acid; or

the substitution of tyrosine-15 of SEQ ID NO: 2 to alanine, histidine-35 of SEQ ID NO: 2 to alanine and asparagine-38 of SEQ ID NO: 2 to aspartic acid.

18. (Amended) The mutant SPE-C toxin of claim 6, wherein the substitutions comprise tyrosine-15 of SEQ ID NO: 2 to alanine and asparagine-38 of SEQ ID NO: 2 to aspartic acid.

19. (Twice Amended) A mutant SPE-C toxin comprising acid substitutions at aspartic acid-12 of SEQ ID NO: 2, tyrosine-15 of SEQ ID NO: 2, tyrosine-17 of SEQ ID NO: 2, histidine-35 of SEQ ID NO: 2, or asparagine-38 of SEQ ID NO: 2.

20. (Amended) A mutant SPE-C toxin comprising amino acid substitution at aspartic acid-12 of SEQ ID NO: 2.

21. (Amended) The mutant SPE-C toxin of claim 20, comprising substitution of alanine for aspartic acid-12 of SEQ ID NO: 2.

22. (Amended) A mutant SPE-C toxin comprising amino acid substitution at asparagine-38 of SEQ ID NO: 2.

23. (Amended) The mutant SPE-C toxin of claim 22, comprising substitution of aspartic acid for asparagine-38 of SEQ ID NO: 2.

24. (Amended) A mutant SPE-C toxin comprising amino acid substitutions at tyrosine-15 of SEQ ID NO: 2 and at asparagine-38 of SEQ ID NO: 2.

25. (Amended) The mutant SPE-C toxin of claim 24, comprising substitutions of serine or alanine for tyrosine-15 of SEQ ID NO: 2 and aspartic acid for asparagine-38 of SEQ ID NO: 2.

26. (Amended) The mutant SPE-C toxin of claim 24, comprising substitutions of serine for tyrosine-15 of SEQ ID NO: 2 and serine for asparagine-38 of SEQ ID NO: 2.

27. (Amended) The mutant SPE-C toxin of claim 24, further comprising amino acid substitution at histidine-35 of SEQ ID NO: 2 .

28. (Amended) The mutant SPE-C toxin of claim 27, comprising substitutions of alanine for tyrosine-15 of SEQ ID NO: 2, alanine for histidine-35 of SEQ ID NO: 2, and aspartic acid for asparagine-38 of SEQ ID NO: 2.

29. (Amended) A mutant SPE-C toxin comprising amino acid substitutions at tyrosine-17 of SEQ ID NO: 2 and at asparagine-38 of SEQ ID NO: 2.

30. (Amended) The mutant SPE-C toxin of claim 29, comprising substitutions of serine or alanine for tyrosine-17 of SEQ ID NO: 2 and aspartic acid for asparagine-38 of SEQ ID NO: 2.

31. (Amended) The mutant SPE-C toxin of claim 29, comprising substitutions of serine for tyrosine-17 of SEQ ID NO: 2 and serine for asparagine-38 of SEQ ID NO: 2.

32. (Amended) A mutant SPE-C toxin comprising amino acid substitutions at tyrosine-15 of SEQ ID NO: 2, at histidine-35 of SEQ ID NO: 2, and at asparagine-38 of SEQ ID NO: 2.

33. (Amended) The mutant SPE-C toxin of claim 32, comprising substitutions of alanine for tyrosine-15 of SEQ ID NO: 2, alanine for histidine-35 of SEQ ID NO: 2, and aspartic acid for asparagine-38 of SEQ ID NO: 2.

34. (Amended) A mutant SPE-C toxin comprising amino acid substitutions at aspartic acid-12 of SEQ ID NO: 2, at tyrosine-15 of SEQ ID NO: 2, at tyrosine-17 of SEQ ID NO: 2, at histidine-35 of SEQ ID NO: 2, at asparagine-38 of SEQ ID NO: 2, or at up to three of these amino acids.

35. (Amended) The mutant SPE-C toxin of claim 34, comprising substitutions of serine or alanine for tyrosine-15 of SEQ ID NO: 2 and aspartic acid for asparagine-38 of SEQ ID NO: 2.

36. (Amended) The mutant SPE-C toxin of claim 34, comprising substitutions of serine or alanine for tyrosine-17 of SEQ ID NO: 2 and aspartic acid for asparagine-38 of SEQ ID NO: 2.

37. (Amended) The mutant SPE-C toxin of claim 34, comprising substitutions of serine for tyrosine-15 of SEQ ID NO: 2 and serine for asparagine-38 of SEQ ID NO: 2.

38. (Amended) The mutant SPE-C toxin of claim 34, comprising substitutions of serine for tyrosine-17 of SEQ ID NO: 2 and serine for asparagine-38 of SEQ ID NO: 2.

39. (Amended) The mutant SPE-C toxin of claim 34, comprising substitutions of alanine for tyrosine-15 of SEQ ID NO: 2.

40. (Amended) The mutant SPE-C toxin of claim 34, comprising substitutions of alanine for tyrosine-15 of SEQ ID NO: 2, alanine for histidine-35 of SEQ ID NO: 2, and aspartic acid for asparagine-38 of SEQ ID NO: 2.

41. (Amended) The mutant SPE-C toxin of claim 34, comprising substitutions of aspartic acid for asparagine-38 of SEQ ID NO: 2.

42. (Amended) The mutant SPE-C toxin of claim 34, comprising substitutions of alanine for aspartic acid-12 of SEQ ID NO: 2.

Please add new claims 43-92 as follows.

43. (New) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an isolated polypeptide with at least 97.5% identity to SEQ ID NO: 2; and
an amino acid substitution at aspartic acid-12.

44. (New) The mutant SPE-C toxin of claim 43, wherein the amino acid substitution comprises:

the substitution of aspartic acid-12 to alanine.

45. (New) The mutant SPE-C toxin of claim 43, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

46. (New) The mutant SPE-C toxin of claim 43, wherein the isolated polypeptide comprises 100% identity to SEQ ID NO: 2 at positions other than aspartic acid-12.

47. (New) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an isolated polypeptide with at least 97.5% identity to SEQ ID NO: 2; and
an amino acid substitution at tyrosine-15.

48. (New) The mutant SPE-C toxin of claim 47, wherein the amino acid substitution comprises:

the substitution of tyrosine-15 to alanine or serine.

49. (New) The mutant SPE-C toxin of claim 47, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

50. (New) The mutant SPE-C toxin of claim 47, wherein the isolated polypeptide comprises 100% identity to SEQ ID NO: 2 at positions other than tyrosine-15.

51. (New) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an isolated polypeptide with at least 97.5% identity to SEQ ID NO: 2; and


an amino acid substitution at tyrosine-17.

52. (New) The mutant SPE-C toxin of claim 51, wherein the amino acid substitution comprises:

the substitution of tyrosine-17 to alanine or serine.

53. (New) The mutant SPE-C toxin of claim 51, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

54. (New) The mutant SPE-C toxin of claim 51, wherein the isolated polypeptide comprises 100% identity to SEQ ID NO: 2 at positions other than tyrosine-17.

 55. (New) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an isolated polypeptide with at least 97.5% identity to SEQ ID NO: 2; and


an amino acid substitution at histidine-35.

56. (New) The mutant SPE-C toxin of claim 55, wherein the amino acid substitution comprises:

the substitution of histidine-35 to alanine.

57. (New) The mutant SPE-C toxin of claim 55, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

58. (New) The mutant SPE-C toxin of claim 55, wherein the isolated polypeptide comprises 100% identity to SEQ ID NO: 2 at positions other than histidine-35.

 59. (New) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an isolated polypeptide with at least 97.5% identity to SEQ ID NO: 2; and

an amino acid substitution at asparagine-38.

60. (New) The mutant SPE-C toxin of claim 59, wherein the amino acid substitution comprises:

the substitution of asparagine-38 to alanine, aspartic acid, or serine.

61. (New) The mutant SPE-C toxin of claim 59, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

62. (New) The mutant SPE-C toxin of claim 59, wherein the isolated polypeptide comprises 100% identity to SEQ ID NO: 2 at positions other than asparagine-38.

63. (New) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an isolated polypeptide with at least 97.5% identity to SEQ ID NO: 2; and
an amino acid substitution at lysine-135.

64. (New) The mutant SPE-C toxin of claim 63, wherein the amino acid substitution comprises:

the substitution of lysine-135 to aspartic acid.

65. (New) The mutant SPE-C toxin of claim 63, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

66. (New) The mutant SPE-C toxin of claim 63, wherein the isolated polypeptide comprises 100% identity to SEQ ID NO: 2 at positions other than lysine-135.

67. (New) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an isolated polypeptide with at least 97.5% identity to SEQ ID NO: 2; and
an amino acid substitution at lysine-138.

68. (New) The mutant SPE-C toxin of claim 67, wherein the amino acid substitution comprises:

the substitution of lysine-138 to aspartic acid.

69. (New) The mutant SPE-C toxin of claim 67, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

70. (New) The mutant SPE-C toxin of claim 67, wherein the isolated polypeptide comprises 100% identity to SEQ ID NO: 2 at positions other than lysine-138.

71. (New) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an isolated polypeptide with at least 97.5% identity to SEQ ID NO: 2; and
an amino acid substitution at tyrosine-139.

72. (New) The mutant SPE-C toxin of claim 71, wherein the amino acid substitution comprises:

the substitution of tyrosine-139 to alanine.

73. (New) The mutant SPE-C toxin of claim 71, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

74. (New) The mutant SPE-C toxin of claim 71, wherein the isolated polypeptide comprises 100% identity to SEQ ID NO: 2 at positions other than tyrosine-139.

75. (New) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an isolated polypeptide with at least 97.5% identity to SEQ ID NO: 2; and
an amino acid substitution at aspartic acid-142.

76. (New) The mutant SPE-C toxin of claim 75, wherein the amino acid substitution comprises:


the substitution of aspartic acid-142 to asparagine.

77. (New) The mutant SPE-C toxin of claim 75, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

78. (New) The mutant SPE-C toxin of claim 75, wherein the isolated polypeptide comprises 100% identity to SEQ ID NO: 2 at positions other than aspartic acid-142.

79. (New) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an isolated polypeptide with at least 97.5% identity to SEQ ID NO: 2; and
an amino acid substitution at tyrosine-15 and asparagine-38.

 80. (New) The mutant SPE-C toxin of claim 79, wherein the amino acid substitution comprises:

the substitution of tyrosine-15 to serine; and
the substitution of asparagine-38 to serine.

81. (New) The mutant SPE-C toxin of claim 79, wherein the amino acid substitution comprises:

the substitution of tyrosine-15 to alanine; and
the substitution of asparagine-38 to alanine or aspartic acid.

82. (New) The mutant SPE-C toxin of claim 79, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

83. (New) The mutant SPE-C toxin of claim 79, wherein the isolated polypeptide comprises 100% identity to SEQ ID NO: 2 at positions other than tyrosine-15 and asparagine-38.

84. (New) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:


an isolated polypeptide with at least 97.5% identity to SEQ ID NO: 2; and
an amino acid substitution at tyrosine-17 and asparagine-38.

85. (New) The mutant SPE-C toxin of claim 84, wherein the amino acid substitution comprises:

the substitution of tyrosine-17 to serine; and
the substitution of asparagine-38 to serine.

86. (New) The mutant SPE-C toxin of claim 84, wherein the amino acid substitution comprises:

the substitution of tyrosine-17 to alanine; and
the substitution of asparagine-38 to alanine.

 87. (New) The mutant SPE-C toxin of claim 84, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

88. (New) The mutant SPE-C toxin of claim 84, wherein the isolated polypeptide comprises 100% identity to SEQ ID NO: 2 at positions other than tyrosine-17 and asparagine-38.

89. (New) A mutant Streptococcal pyrogenic exotoxin type C (SPE-C toxin) comprising:

an isolated polypeptide with at least 97.5% identity to SEQ ID NO: 2; and
an amino acid substitution at tyrosine-15, histidine-35, and asparagine-38.

90. (New) The mutant SPE-C toxin of claim 89, wherein the amino acid substitution comprises:

the substitution of tyrosine-15 to alanine;
the substitution of histidine-35 to alanine; and
the substitution of asparagine-38 to aspartic acid.

91. (New) The mutant SPE-C toxin of claim 89, wherein the percentage identity to SEQ ID NO: 2 is at least 99%.

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92. (New) The mutant SPE-C toxin of claim 89, wherein the isolated polypeptide comprises 100% identity to SEQ ID NO: 2 at positions other than tyrosine-15, histidine-35, and asparagine-38.
